

REMARKS

Claims 1-5, 7 and 9-18 remain in this application and are rejected. Claims 2, 6 and 8 are previously canceled. Claims 1, 12 and 13 are amended herein.

The Examiner objects to the drawings under 37 C.F.R. § 1.83(a) for failing to show every feature of the invention specified in the claims. It is stated that the drawings do not show the rigid frame with an array of holes according to claim 12. Please find accompanying this amendment new Figs. 3-5. No new matter is added since the features of the new drawings are clearly supported by the specification and the above noted claim. The specification is amended to properly reference the drawings. The portion of the text of the specification which supports the drawings is found on page 11 of the substitute specification. In view of this addition, reconsideration of the objection to the drawings and withdrawal thereof are earnestly solicited.

Claims 1, 3-5, 7 and 9-11 are rejected as obvious over the Tretyakov reference in view of the Dannoux reference under 35 U.S.C. §103(a). The applicant herein respectfully traverses this rejection. For a rejection under 35 U.S.C. §103(a) to be sustained, the differences between the features of the combined references and the present invention must be obvious to one skilled in the art.

It is respectfully submitted that a *prima facie* case of obviousness could not be established in rejection of amended claims 1, 3-5, 7 and 9-11. "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)." MPEP §706.02(j) "Contents of a 35 U.S.C. §103 Rejection".

Claim 1 is now amended to include the subject matter of claim 12 relating to the support frame having an array of holes. Claim 12 was previously rejected based on the above noted references further in view of the Sanadi reference.

Applicants respectfully submit that the prior art lacks the suggestion to make the combination proposed by the Examiner. It is well settled that features of prior art references may not be assembled to establish obviousness using the pending claims as a template. Indeed, the court in *In re Fritch*, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992) stated that "[t]he mere fact that the prior art may be

modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." Thus, the prior art references must suggest some desirable attribute for making the proposed combination and not just provide an alternative possibility for an assembled assortment of features. The Examiner has merely set forth a possible combination of different features but has failed to show how the references suggest such a combination. Absent such a showing, the obviousness rejection is not sufficiently support to establish a *prima facie* case of obviousness.

The inclusion of a rigid support frame with a plate formed of thin flexible film having an array of wells is not suggested by the art references cited because the incentive to include a frame in the well plate of the Tretyakov reference is absent. In the Tretyakov reference the well plate is formed by vacuum forming directly in the heat block of the thermocycler. The bottom of the wells in the heat block have apertures for applying the negative pressure for forming. Once the wells are formed, the PCR operation is performed in the wells of the thin flexible film plate directly in the heat block used to form the wells. Accordingly, the Tretyakov reference does not require a support frame since the heat block functions to support the thin flexible film plate of wells. Nothing in this reference teaches a need for a support frame or even suggests a reason for one to remove the thin film well plate from the heat block prior to completion of its use in PCR

thermocycling. In other words, there is no incentive taught for one to add extra steps to the method of the Tretyakov reference involving transport of the thin flexible film well plate prior to its use.

Clearly the Tretyakov reference provides a complete method for PCR cycling. No rigid frame is needed in the process. One need not remove the thin film well plate prior to completion of the process. Thus, there is no need to provide a rigid frame with the thin flexible film well plate which is completely supported by the heat block.

The Examiner has cited the Dannoux reference for teaching a support frame. However, the Dannoux reference teaches a device wherein wells are formed with clear bottoms to permit optical inspection of the contents from below. Thus, it is necessary that the well plate be support by a frame to permit moving the well plate to an observation device. The device used to form the wells does not permit observation. On the contrary, the device used to form the well plate in the Tretyakov reference permitted the entire PCR cycling to be done in the heat block having the vacuum apertures. Therefore, one skilled in the art would see no need to remove a multiwell plate prior to completion of the process. Hence, it is respectfully submitted that the incentive to arrive at the claimed invention is absent from the references.

The claimed invention is further patentable because the applicant has identified a source of a problem not heretofore known. The use of the thin film plate allowed increased speed in the PCR process. However, the present application has identified that speed could be further increased. It is only the present application which has identified a problem and a source of a problem with the system of the Tretyakov reference which would lead one to its modification. In particular, the apertures in the well bottoms limit heat transfer and therefore PCR cycling speed. Absolutely nothing in the art cited identifies such a deficiency.

Nonobviousness may be clearly shown where an inventor seeks to remedy a known problem, and does so by discovering a heretofore unknown source of the problem and finds a solution based upon the discovery of the problem source. *Eibel Process Co. v. Minnesota and Ontario Paper Co.*, 261 U.S. 45 (1923). In the present application, the applicant as both identified a problem and determined its source.

In *Eibel Process* the plaintiff discovered that by increasing the pitch of the wire mesh in the Fourdrinier paper making machine it was possible to increase paper production significantly. The plaintiff had identified the source of the problem in previous attempts in increasing production as the speed differential of paper making stock and the wire mesh. Similarly, the present applicant has identified that the apertures in the wells which permitted ultrathin film wells to be

formed allowing faster PCR cycling, simultaneously create an impediment. Thus, the applicant has incorporated a rigid frame in the thin film multiwell plate to permit its transport to a heat block without vacuum apertures.

Claim 1 further recites that the rigid frame has an array of holes. The Examiner submits that the Sanadi reference teaches such an array. The Sanadi reference shows a support plate with an array of holes for accepting individual sample vessels. However, one would not arrive at the proposed combination of references because the plate of Sanadi is used to support the vessels in a spaced relationship. Since the wells of the well plate of the present invention are formed in a spaced relationship, there is no incentive to use a support plate with an array of holes.

The Examiner suggests that it would obvious to use the Sanadi arrangement because it is an *alternative*. As note above, the prior art references must suggest some desirable attribute for making the proposed combination and not just provide an alternative possibility for an assembled assortment of features. *In re Fritch*. Absent such a showing, the obviousness rejection is not sufficiently support to establish a *prima facie* case of obviousness. It is necessary to show the references teach a desired reason for using the alternative.

Claims 13-18 are rejected under 35 U.S.C. §103(a) as obvious over the Tretyakov reference in view of the Dannoux reference and further in view of the

Atwood '381 reference. Claim 13 incorporates the apertureless heat block in the body of the claim so it is considered in combination with the well plate and frame. The Tretyakov reference only teaches using the well plate in a heat block with holes in the wells for applying the vacuum to form the wells in the well plate *as well as for* conducting the PCR thermocycling. This is because the well plate is flexible and too thin to support itself outside of the heat block. Accordingly, all necessary operations may be conducted in the heat block having the wells with apertures in the bottoms.

As noted above with respect to the rejection of claim 1, there is nothing in the art providing incentive to change this arrangement since it is fully functional and there is no identification of a deficiency in the arrangement. As emphasized above, it is only the present disclosure which would provide incentive to arrive at the claimed arrangement of claim 13.

In contrast to the Tretyakov reference, the Atwood '381 reference teaches using an apertureless heat block with standard individual sample tubes which are self supporting. Since, the Tretyakov reference only teaches using the thin multi-well plate in the forming block itself where both forming and PCR cycling are conducted, there is no suggestion to apply it to an apertureless heat block because all functions are accomplished in the forming block. Furthermore, since the multi-well plate is so thin as to be difficult to transport, one would be dissuaded from

attempting such use because transferring without a support frame is not practical. Again, nothing in the art shows it is more desirable to transfer the plate before PCR cycling. In contrast, the Sanadi reference requires removal of the well plate formed in the forming device for its use. Hence, the frame is dictated by the method of use in the Sanadi reference, which method is clearly dissimilar from that of the Tretyakov reference. Accordingly, the art fails to provide the requisite suggestion to make the proposed combination.

The Examiner has theorized that one would use an apertureless block to allow further plates to be formed during cycling. However, as recited in the Examiner's rejection, such use is considered an "alternative." As noted above, there must be some desirability for an alternative to be used in order to support the combination of references. In view of the fact that the thin flexible film plate is not supportable outside of the forming/cycling block, thereby making movement impractical, and that the complete reaction may be conducted in the forming/cycling block, the proposed incentive to form other well plates while cycling is clearly outweighed by the totality of the difficulties involved. In particular, it is likely that the transfer operation would take more time than the forming of the plate in the first place thereby making the proposed operation undesirable.

Thus, it is respectfully submitted that the rejected claims are not obvious in view of the cited references for the reasons stated above. Reconsideration of the rejections of the claims and their allowance are respectfully requested.

Claims 1, 3-5, 7, 9-11 and 13-18 are rejected under the judicially created doctrine of the "obviousness" type double patenting rejection as unpatentable over claims 1-21 of U.S. Patent No. 6,556,940.

With regard to the "obviousness" type double patenting rejection, the assignee herein files, without prejudice, a terminal disclaimer in compliance with 37 CFR 1.321(b) pursuant to 37 CFR 1.78(d) in order to overcome any such double patenting rejection. Please charge the corresponding fee of \$110.00 to Deposit Account No. 10-1250.

Applicant respectfully requests a one month extension of time for responding to the Office Action. Please charge the fee of \$110.00 for the extension of time to Deposit Account No. 10-1250.

In light of the foregoing, the application is now believed to be in proper form for allowance of all claims and notice to that effect is earnestly solicited. Please charge any deficiency or credit any overpayment to Deposit Account No. 10-1250.

Respectfully submitted,
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enc: New drawing sheet of Figs. 3-5.